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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/873,601	06/12/1997	GARRY P. NOLAN	A-63915/DJB/	2070

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/873,601	NOLAN ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-83* is/are pending in the application.

4a) Of the above claim(s) *58-80 and 82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 58-83 are pending in the application.

Claims 1-57 have been cancelled (not claims 1-58, as stated at page 2 of the instant REMARKS).

Claims 58-80 and 82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species.

Claims 81 and 83 are under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 81 and 83 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

In view of the amendments to the claims, this rejection no longer applies.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 81 and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the last Office action.

Response to Arguments

Applicants submit that what is being claimed is a simple and elegant method for complexing, within a cell, enzymes that would not usually be complexed together. The claim-recited enzymatic complexes are most easily described with reference to Fig. IA, Essentially, an enzymatic complex contains two components: a component containing enzymes and a component containing a scaffold. The enzymes bind to the scaffold via binding sequences in a cell to form an enzymatic complex. This is all that is required to make a claim-recited enzymatic complex. In discussing the level of disclosure required in a patent application, the MPEP is explicitly clear: a patent

specification need not teach, and preferably omits, what is well known in the art. Applicants submit that all of the components necessary for producing enzymatic complexes are well known in the art, and, accordingly, need not be described in any great detail. For example: many thousands of enzymes and their encoding polynucleotides are known and described in the NCBI'S PubMed and Genbank database. In fact, many enzymes of particular interest are listed on page 14, lines 1-18 of the instant specification. Likewise, many hundreds of sites of protein/protein or protein/DNA interactions are well characterized and well known in the art and can be used in the subject methods. Polypeptide scaffolds, at a minimum, contain binding sites complementary to those present on enzymes and can be easily envisioned by a skilled in the art once a particular binding site had been chosen. Further, if it is desirable to use linkers such linkers are also well known and described on page 23, lines 6-23 of the instant specification. Methods of introducing binding sites into polypeptides by recombinant means and methods of introducing nucleic acids into cells have been practiced for years. In summary, a claim-recited enzymatic complex can be produced using methods and components that are well known. Given the massive amount of knowledge of enzymes and interaction sites (e.g., sites of protein/protein interaction),

and the fact that methods for introducing binding sites into polypeptides have been practiced for many years, the Applicants respectfully submit that Fig. IA (or Fig. 3 for that matter), in combination with the detail present in the text of instant specification, is sufficient to show that the inventors possessed the invention.

In response, if the written description were satisfied only by listing all the known components in the art, then the specification amounts to nothing more than a compendium of the components. It is not that these compounds are not known, as applicants admit there are thousands of them. Rather, that the specification lacks a detail description how or which particular compounds can be combined or chosen for the objective method. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See further the recent case decision

University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

If applicants choose to rely upon general knowledge in the art to render his disclosure complete, applicants must show that anyone skilled in the art would have actually possessed the knowledge [In re Lange (CCPA 1981) 644 F2d 856, 209 USPQ 288], or would reasonably be expected to check the source which applicants rely upon to complete his disclosure and would be able to locate the information with no more than reasonable intelligence. This is the more true in view of applicants' allegation that the method is novel. There is no explicit description in the specification as to the method of screening of a single protein-enzyme complex reaction. Thus, not everything which may be cited as prior art to preclude the grant of a patent can be equated with common knowledge for the purposes of meeting the description requirement of 112. Applicants' arguments are as general as the claimed method and the specification disclosure.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards.

In view of the amendments to the claims and applicants' arguments the rejection has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 81 and 83, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Khosla et al (U.S. 6,391,594) for the reasons set forth in the last office action.

Response to Arguments

Applicants acknowledged that Khosla's methods involve a polyketide synthase polypeptide (PKS) having multiple enzymatic domains separated by a scaffold. The domains may be exchanged in order to modulate the enzymatic activities, and produce different polyketides. But argue that Khosla's scaffolds are naturally occurring scaffolds, not non-naturally occurring exogenous scaffolds, as required by the claims. Further, Khosla's describes only enzymatic complexes in which the enzymes and scaffold of the complex are joined together in cis, i.e., in a single fusion polypeptide. Khosla fails to disclose an enzyme complex in which enzymes are bound to a scaffold via binding sequences that are present in the scaffold and enzymes, as required by the instant claims.

In response, it would be within the order the skill in the art to use a non-naturally occurring scaffold, since a non-naturally scaffold functions in the same way as the natural one. The claims recite only a non-natural scaffold. It is not evident from the disclosure whether in fact such scaffold is a non-naturally occurring. Applicants' arguments that the components of Khosla are joined in cis are not commensurate in scope with the claims. The claims can read on a cis binding or fusion of the components.

Claims 81 and 83, as amended, are rejected under 35 U.S.C. 103(a) as being obvious over Nolan [USP 6,365,344].

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an

obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Nolan discloses at col. 2, lines 25-45 a method comprising expressing a molecular library of randomized nucleic acids as a plurality of isolated corresponding randomized expression products in a plurality of cells, each of the nucleic acids comprising a different nucleotide sequence, screening for a cell of the plurality of cells exhibiting a changed physiology in response to the presence in the cell of a transdominant expression product of the corresponding expression products. The expressing step comprises translating the nucleic acids and/or corresponding transcripts, and each of the nucleic acids encodes a peptide comprising a different amino acid sequence. The nucleic acids may be joined to sequences encoding polypeptide backbones of artificial design capable of intracellularly presenting randomized peptides as structured domains. The methods may also involve introducing the library into the cells, such as through the use of retroviral vectors. Nolan discloses at col. 3,line 45 that a partner may be provided which conformationally restricts the randomized expression product to more specifically define the number of structural conformations available to the cell. For example, such a partner may be a synthetic presentation structure: an artificial polypeptide

capable of intracellularly presenting a randomized peptide as a conformation-restricted domain. Generally such presentation structures comprise a first portion joined to the N-terminal end of the randomized peptide, and a second portion joined to the C-terminal end of the peptide. Preferred presentation structures maximize accessibility to the peptide by presenting it on an exterior loop. The randomized expression product region is expressed on the cell surface and presented to the extracellular space, such that it can bind to other surface molecules (affecting their function) or molecules present in the extracellular medium. The binding of such molecules could confer function on the cells expressing a peptide that binds the molecule. The cytoplasmic region could be neutral or could contain a domain that, when the extracellular randomized expression product region is bound, confers a function on the cells (activation of a kinase, phosphatase, binding of other cellular components to effect function). Similarly, the randomized expression product-containing region could be contained within a cytoplasmic region, and the transmembrane region and extracellular region remain constant or have a defined function. See further the Experimental at col. 6. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use an enzyme bound

scaffold or presentation structure since Nolan discloses an enzyme as carboxypeptidase in the Example.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 58-80 and 82 drawn to a nonelected invention. A complete reply to the final rejection

must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
August 6, 2004